any intensive appropriate anti-syphilitic medication, and reject the former on account of the impossibility of regeneration of central and spinal nervous structure. To illustrate: several years ago we had an avowed syphilitic under observation, who presented the classical symptoms of tabes; he was put under a treatment of proto-iodide pills and iodide of potassium, with the result that all the ataxic symptoms disappeared, and have not returned to this day. In tabetic cases then, salvarsan, or any treatment is indicated only if a positive Wassermann is developed and active syphilitic symptoms exist.

There are no exact results in hemiplegia and paraplegia, and the treatment of paresis is always a failure.

This compilation does not include all of the symptoms and lesions of syphilis; it merely contains certain varieties upon which the action of salvarsan has been accurately demonstrated. Because certain lesions disappear rapidly and treponema are destroyed in a few days, the claim is not warranted that the disease is eradicated.

One of the most energetic French writers [6] states: "We have often noted recurrences after single or plural injections; further, the results of the serum reaction are not constant, and positive reactions are frequently obtained even after three doses of salvarsan. What we may say is that if an intensive treatment is instituted, for instance, three intravenous injections of high dosage, all given wthin a period of 3 to 4 weeks, we have not after 5 months seen any recurrences."

Stoker,[7] reporting 700 intravenous injections, says that the duration of the treatment should be intermittent for 3 or 4 years. Neisser [8] advises that it be continued for months and years, until all syphilitic symptoms disappear permanently, and a permanent negative Wassermann reaction is obtained. He is not prepared to say what is the therapeutic and prognostic value of the Wassermann, and maintains that salvarsan has complicated the treatment of lues.

It does not follow that certain cases may not receive but one injection, and that intramuscularly, and remain free from recurrence even after a year; but we cannot feel secure, considering the vagaries of the serum reaction, in honestly assuring our patients, at least up to the present, that they are free from infection, and permit them to take on such a responsibility as marriage.

What can be hoped for the recipient of salvarsan, if one injection only is considered sufficient in certain cases, and plural injections are necessary in others? In the commerce of medical practice, we would not dare to tell any one private patient that perhaps from 5 to 10 injections may be necessary to cure him. This might do in institutional work, where heroism is more casual than riches.

In résumé then, we agree that arsenobenzol has its field of usefulness, that in certain cases it gives surprisingly good results, that its most potent action is upon lesions in active evolution, and that in some cases it surpasses mercury in rapidity of effect.

But we contend that alone it has not positive curative power, because sufficient time has not elapsed to prove its permanent efficacy; and recurrences of symptoms and lesions seen after one, may well be seen after plural injections. It has not positive abortive action, and further the inconstancy of the sero-reaction makes of it an enigma, the solving of which will perhaps be perceived in the future.

In any case we are not authorized to consider a patient definitely cured. The mercurial treatment, methodic, intermittent and prolonged, should always be instituted after arsenobenzol. Under the existing circumstances, it can neither exclude nor replace the former.

In conclusion we suggest that it is the duty of the profession to enlighten the laity, and protect them by conscientious advice, and truthful facts.

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SALVARSAN IN VARIOUS MEDICAL DISORDERS ASSOCIATED WITH A WASSERMANN REACTION.*

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It is the object of this paper to review the cases seen in the Medical Wards of Lane Hospital between January 1, 1911, and April 1, 1912, where a Wassermann reaction was present and salvarsan was given. For keeping the records of these patients much is due to the assistance of Dr. P. H. Luttrell, to whom acknowledgment is herewith gratefully made. To call these cases visceral syphilis is not altogether accurate, because they include manifestations in structures not correctly defined as viscera; and because even where viscera seemed involved none of these patients came to autopsy to confirm the suspicion. The cases observed and herewith presented number 51 in all; but many of these had salvarsan more than once, so that the total number of injections considerably exceeds this figure.

In classifying these, the largest group, as might be expected, has been that involving the nervous system. In this there have been 23. These neurological cases with Wassermann reaction have been studied especially by Dr. W. F. Schaller, who has taken up their consideration in detail in a separate paper; and they will therefore not be dealt with in this. Suffice it to say that they include affections of all parts of the nervous system—brain, spinal cord and peripheral nerves.

The next largest group has been that where the diagnosis made by patients themselves has been

* Read before the Forty-Second Annual Meeting of the State Society; Del Monte, April, 1912.

rheumatism; of such cases there have been 9. These patients have complained especially of pains in joints, or in bones between joints, or in muscles and fasciae; these pains persisting for months or for years, but usually without visible evidence on examination, of redness or swelling or alteration in contour; though often there was tenderness or stiffness on moving the joints or limb of which complaint was made. In one case there was found a hydrops of the knee, the fluid aspirated as well as the blood from the arm showing the Wassermann reaction. In two cases there was a history of chronic gonorrhea as well as of lues, and the suspicion of gonorrheal arthralgia was strong enough to prompt the use of gonococcic vaccine; but in each case the greater relief seemed to follow the injection of salvarsan. These pseudo-rheumatic patients all claimed to be greatly benefited by the salvarsan; though in several the pains recurred after a variable interval and the injection had to be repeated.

Next in frequency come the cases where the complaint was of stomach trouble. Out of the large number of patients with this story to tell, there were five who gave the Wassermann reaction. In two of these it was possible to demonstrate the existence of tabes dorsalis and to classify the "stomach trouble" as gastric crises. In both of these stomach analysis showed hyperchlorhydria and in one of them a persistent hypersecretion. Salvarsan gave both much relief. Two of the other cases, without evidence of tabes, likewise had hyperchlorhydria to explain their gastric symptoms; while the remaining one was clinically chronic gastritis with subacidity. It is impossible in such cases to conclude, simply because a Wassermann reaction is coincident, that syphilis is the cause of the symptoms; and as salvarsan accomplished no permanent benefit in any of the three, the best proof is afforded that some other cause existed. The chronic gastritis case was given this remedy on November 3rd with no improvement following; again on November 27th with temporary improvement; but in March, 1912, he was back again with all his old symptoms and a triple X Wassermann in spite of his two injections; so a third was given on March 20th. One of the hyperchlorhydria cases had a tender appendix that was probably the source of his dyspepsia. Salvarsan gave him only temporary relief, probably subjective. The other case was not at all relieved by the injection, though the Wassermann reaction subsequently became negative.

Cases of intestinal trouble have been more infrequent and only two have been seen with coincident positive Wassermann reaction. One of these was an obstinate constipation of several months' duration with no discoverable abnormality in abdomen, rectum, stomach contents or feces. After salvarsan he undoubtedly improved in a remarkable way, his bowels moving regularly without laxatives or other aid. The second was a case of dysentery, with pain in the left side of his abdomen and mucus and blood in his stools at intervals for over a year; with visible ulcers just beyond the internal sphincter; no amebae in his feces, nor tubercle bacilli; but a positive Wassermann reaction. After salvarsan his ulcers healed, his symptoms all disappeared and he left the ward perfectly well.

As regards the liver, which is supposed to be a frequent sufferer in chronic syphilitic infection, we have had but two cases where the symptoms and signs pointed to this organ and where the Wassermann was found. One of these presented a rather characteristic history of chronic gall-bladder disease, with recurring attacks of colic and jaundice; after salvarsan, her long-standing symptoms all disappeared, but whether permanently remains to be seen. In the other case, with deep jaundice and a greatly enlarged smooth liver but no pain, salvarsan given twice has so far produced no effect and it seems probable that the disease is malignant, and not explained by the blood reaction for syphilis.

The respiratory system has only twice presented symptoms coincident with Wassermann reaction. One case ill for two months with hoarseness, cough and loss in weight suggested tuberculosis; but the lungs were found normal and the sputum showed no bacilli; while the larynx showed diffuse infiltration of the whole mucous membrane, hyperemia of the cords and the right cord swollen and indurated; and the blood showed a positive Wassermann. After salvarsan there was decided improvement in his voice, his general health and his larynx. The second case complained of chronic cough and expectoration and his chest presented the signs of chronic bronchitis; after one injection of salvarsan his condition improved remarkably in every way, he lost his cough, gained in weight, and his Wassermann reaction became negative.

It is rather surprising that we have seen but two cases of disease of the circulatory system, with coincident Wassermann reaction. One of these presented the clinical picture of general arteriosclerosis with myocarditis and broken compensation. Salvarsan was given him but once and then in half dose, because the condition seemed too critical to warrant more; no effects either good or bad followed, that could be attributed to the injection. The other case was one of aortic regurgitation with broken compensation and extensive dropsy. He was never given salvarsan because too ill to justify it; and his case is therefore not included in the number reported.

Of the remaining cases, various clinical manifestations were associated with the Wassermann reaction; in one an extensive stomatitis and glossitis, cured promptly by one injection; in one, multiple recurrent boils, also much improved after salvarsan; and in two, chronic disturbances of the eyes, with conjunctivitis, iritis and retino-chroiditis, improved but not cured after treatment.

Infectious fever: As syphilis belongs to the group of specific infectious diseases, it is not surprising that at times it presents a fever course and symptoms that make it resemble other more acute infections. In such cases the Wassermann reaction may or may not be of aid in differential diagnosis; for on the one hand it may be absent even though the symptoms are due to syphilis; and on the other, it may be present even though the symptoms are

due to some other coincident infection. In illustration of the difficulties about deciding what a negative or positive Wassermann reaction really means, the great good that salvarsan may do if indicated and the uselessness or even harm in its administration if not indicated, the three following cases have seemed the most interesting of all we have to present, and are therefore described in detail.

Case 1. A man, age 42, a laborer by occupation, was admitted February 24, 1911, complaining of headache and no appetite, for two weeks previous with gradually increasing weakness and loss in weight. He admitted gonorrhea but positively denied syphilis. On admission his skin showed no eruption except slight acne over his back. His throat was reddened, the posterior wall inflamed and covered with mucus but the tonsils were not enlarged and there were no deposits or ulcerations. No abnormality was found in his lungs, heart or abdomen; no enlargement of liver or spleen; no enlarged lymphatic glands; no edema of extremities or scars. His temperature from the beginning was slightly elevated, from 99° to 101°.

Gradually during March he developed enlargement and bogginess of the tonsils, and increased inflammation of the throat, with ulcers on the pharyngeal wall, the pillars of the fauces and both tonsils; all of them covered by a whitish membrane, all raised and irregular and with grandular surface, and all very painful and tender. The laryngeal mucous membrane likewise became infiltrated, edematous and reddened; with several pinhead-sized yellow areas resembling tubercles. During the development of these throat lesions the temperature pursued a low course, at times normal in the morning, rarely rising above 101° in the evening and never above 102°.

But by the beginning of April, coincident with extensive ulcerations and membranous deposit in the throat, the temperature became continuous at a higher level, averaging 101° to 102°, without morning remission and with occasional evening rise to 103° or 104°. The pulse rate likewise gradually rose from normal until it averaged 120. At this time also the patient developed a general skin eruption. The clinical note made on April 3rd says: "Over forehead, cheeks and chin there are numerous discrete papules and pustules and a few macules; the eyelids are reddened, thickened and bathed with a sero-purulent discharge; the ocular conjunctivae are slightly injected; each nostril is reddened and inflamed and partially occluded by purulent discharge; the lips are pale, both are swollen and the lower lip shows several of the maculo-papular lesions seen elsewhere on the face; the breath is very offensive, the tongue heavily coated; the roof of the mouth shows numerous reddened, infiltrated areas, like purpuric spots; the teeth are decayed, several are missing, all show abundant thick deposit at the junction of the gums; both tonsils and the posterior wall of the pharynx are completely covered by a grayish-yellow deposit; the expectoration is profuse, viscid and bloody; cervical glands are moderately enlarged on both sides; over right forearm and arm there are numerous discrete lesions resembling those on the face, except that more of them are macular and on the forearm they are distinctly purpuric in character; over the left forearm and extending half-way between elbow and shoulder there is a diffuse blotchy, purpuric discoloration; between the elbow and shoulder several discrete maculo-papular lesions are seen; the right hand shows numerous macules, and the right wrist is stiff and painful; the left hand is swollen, edematous and the fingers and wrist are likewise stiff and painful, with a few macules found on the dorsum of the hand; over both lower limbs numerous purpuric spots are found, but discrete and scattered and nowhere confluent; no skin lesions are found at this time over the trunk, except a few fine spots in each axilla, no abnormality is found in lungs, heart or abdomen, except that the area of liver dullness measures 14 cm. and that of the spleen 7 cm."

During April the patient's general condition grew steadily worse; his temperature and pulse rate ranged persistently high, and he lost rapidly in weight and vitality. The throat condition showed no improvement. The skin lesions gradually developed into large pustules, thickly scattered over both sides of the face and scalp, the ears and neck, both arms, both legs, the back and the upper part of the trunk; they varied in size from a pea to a half dollar; all had thick crusts, "piled up" like the classical rupia.

The effort to identify the nature of this patient's illness caused much investigation by various men in the hospital ward and laboratories. It was clear that he was suffering from some chronic infection, the only question being as to its character. At the outset, diphtheria was the first thought, but this possibility was soon eliminated by cultures from the throat. The next hypothesis was that of streptococcus infection, a theory that seemed to be proven when streptococci grew in the cultures from throat swabs; but anti-streptococcic serum given twice in the latter part of March had no effect, except perhaps to cause some of the purpuric eruption and the joint pains that developed soon afterwards. Tuberculosis of the throat was eliminated by the persistent failure to find tubercle bacilli in the sputum or in swabs from the ulcerated surfaces. Glanders seemed a very likely explanation of the naso-pharyngeal lesions, the fever, the skin eruption and the arthritis; but throat cultures and blood cultures and cultures from the pus underneath the crusts on the skin all failed to show the characteristic organism; injections of guinea pigs were likewise without diagnostic results; the injecton of mallein gave no reaction; and it was thus at last found impossible to verify the suspected diagnosis of glanders.

At the outset and as the case developed, syphilis seemed a most likely explanation of the fever, the throat condition, the tender joints and especially the skin lesions. But the patient insistently denied this possibility; and furthermore, what seemed particularly conclusive, the Wassermann reaction was negative, not only once but on three different occasions during the course of the investigation. Nevertheless, as the patient steadily grew weaker and more emaciated and his death seemed inevitable; and as no other diagnosis had been established as a basis for treatment, it was finally concluded to give salvarsan anyway, on the clinical evidence, in spite of the negative Wassermann reaction. The first dose, .6 gram was administered intravenously on May 15th. Within twenty-four hours the temperature fell from 103° to 99°, and never again went above 100°. The patient at once improved, both subjectively and objectively and in a way that seemed almost magical. The large pustular crusts on the skin dried up and fell away; the mouth and throat became clear; the appetite returned and the patient began to gain in weight. Ten days after salvarsan was given, the blood showed a triple X positive Wassermann reaction, conclusively demonstrating the nature of the infection. On June 20th a second dose of salvarsan was given, although the patient then showed practically no signs of his previous illness and was up and walking about the ward. He left the hospital on August 10th absolutely well, strong and fat and ready to return to work.

Case 2. A man, age 23, a laborer, was admitted to the hospital September 23, 1911, complaining of sore eyes, headache, and pains in his legs. He had a history of gonorrhea two years before and again eight months later; and since the second attack a

chronic gleet, with characteristic "morning drop." One year before he had what was diagnosed as soft chancre, that healed up in one week; without any subsequent rash or sore throat or other evidence of disease.

His present illness began five days before, with inflammation of his eyes and watery discharge. The next day headache began in the temporal regions and he had pains all over his body, but principally in his arms, back and legs. On admission his temperature was 102° and fever persisted thereafter, ranging each day from 100° a. m. to 102° p. m. His eyes showed a conjunctivitis, iritis and irido-cyclitis. His tongue was coated. The glands on each side of the neck, in each submaxillary region and each post-auricular region, were enlarged and palpable. There was no abnormality found in lungs or heart. The liver was slightly enlarged and the area of splenic dullness measured 8 cm. The abdomen was slightly distended and distinct rigidity was found in the right side, with tenderness, in the region of the caecum. The urine showed a light cloud of albumen and many leucocytes, but no casts.

The first question that arose was whether this man's infection was by typhoid bacilli, for which the fever, the headache, the enlarged spleen, the distended abdomen and the tenderness in right iliac fossa all spoke. But on the other hand, typhoid would not explain the inflammation of his eyes or his enlarged glands. On blood examination he was found to have 10,000 leukocytes with 75 per cent. polymorphonuclears; the Widal reaction was negative, and blood cultures were likewise negative.

Measles in the pre-eruptive stage might explain all the symptoms, but it seemed that days enough had elapsed since onset for the eruption to appear; furthermore, no other mucous membranes but those of the eyes were involved.

Smears from the meatus urethrae showed gonococci present and the history indicated the existence of a chronic gonorrhea; from which his eyes might have been infected or even a general sepsis might have arisen.

But the real clue to the nature of the infection was furnished by a triple X Wassermann reaction, indicating an active syphilitic process; and on this theory salvarsan was administered on September 28th, five days after admission. The effect was miraculous. In twelve hours the temperature fell to normal and the fever never recurred. The iritis disappeared; the enlarged glands shrank to normal size; the pains in head and limbs all vanished, and four days after salvarsan was given the patient left the hospital, feeling and appearing in perfect health.

Case 3. It was inevitable that two such brilliant successes should cause over-confidence and so lead to disaster. It followed very shortly. On October 24th, 1911, a man aged 46 was seen at the out-patient clinic with a history that for three or four weeks he had entirely lost his appetite, had lost fifteen pounds in weight, his bowels had been very constipated and he had occasional headaches. He had a definite chancre three years before, followed by symptoms that he had been told were "secondaries"; but he was treated for only five or six weeks, by inunctions and medicine internally. On examination he was found to have a coated tongue; liver and spleen enlarged and palpable; a tender mass in the right side of abdomen over the cecum; palpable epitrochlear glands; marked peripheral arterio-sclerosis; numerous scars and several open, bleeding ulcers on both shins. His blood gave a positive triple X Wassermann reaction on October 26th. On admission to the hospital he was found to have a temperature ranging from 99° to 101° each day. On November 1st he was given salvarsan intravenously, without reaction—no chill, no rise of temperature, no nausea or vomiting. On November 3rd at 4 p. m. he had slight epistaxis; this recurred after midnight and became so profuse that it necessitated packing of the naso-pharynx on the morning of the 4th; even after that persistent oozing continued during the 4th and 5th. On the evening of the 5th he had a copious bloody discharge from the bowel. On the 6th he seemed better and lost no blood; but on the 7th he had several large tarry stools, four in all; on the 8th there were two bloody passages. On the 9th the tarry stools continued; an oozing from the nose recurred; a bloody discharge began from the mucous membranes in mouth and from the gums; and he coughed and expectorated blood. On the 10th bleeding continued from nose, mouth, bronchial mucous membrane and bowel; and on the 11th he had in addition a hemorrhage from one of the ulcers on his leg. This went on until his death at 5 p. m. on the 12th.

As bleeding began and persisted the temperature for the first three days rose slightly, but after that gradually fell; but the pulse rate steadily rose from 100 to 150. As the case progressed the patient became rapidly weakened, with drowsiness most of the time, involuntary bowel movements, labored respirations and occasional delirium. The urine at the outset was normal in quantity and quality; in the out-patient department before admission and in the hospital after admission, for the first week; then it began to show albumen and a large number of granular casts. The blood became rapidly depleted as the hemorrhages went on. On November 8th the hemoglobin was 20 per cent., the red corpuscles 1,250,000, the white corpuscles 4,800; on November 10th the hemoglobin was 18, reds 1,100,000, whites 6,000. The red cells showed all the evidences of rapid anemia, in poikilocytosis, anisocytosis, and polychromatophilia, with the presence of a few nucleated reds. The coagulation time averaged 10½ to 11 minutes.

The medical therapy, besides the local treatment to the naso-pharynx by packs and astringents, included calcium chloride by mouth; horse serum repeatedly, subcutaneously and intravenously; human blood serum intravenously; normal salt solution under the skin, in the bowel by the Murphy drip, and intravenously; tincture of iron by mouth; strychnine hypodermically; gelatin solution by mouth and by bowel. The patient was seen by practically every member of the medical, surgical and rhinological staffs in the hospital, and every suggestion that offered any prospect of relief was faithfully tried; but all without success.

By those who watched this case the bleeding was supposed to be due to the administration of salvarsan and to no other cause. The autopsy, however, showed all the characteristic pathology of typhoid fever; this was the active disease that had caused the symptoms and the Wassermann reaction was only an incident of the earlier luetic infection. It follows that salvarsan was not indicated in this illness, and it seems highly probable that it really contributed to the fatal outcome.

CONCLUSIONS.

First: The finding of evidence of visceral disease plus the finding of a Wassermann reaction does not necessarily mean syphilitic disease of the organ giving the symptoms.

Second: The existence of chronic syphilitic infection, as manifested by a positive Wassermann reaction, does not confer immunity against any other organic or infectious disease; and any disorder may occur with it that may occur without it.

Third: The administration of salvarsan may remove a Wassermann reaction but have no beneficial effect on the patient's symptoms or general condition; in fact, may make him worse instead of better, when these symptoms are really due to some other cause than syphilis.

(The Symposium on Syphilis will be concluded in the October issue.)